

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
9 June 2005 (09.06.2005)

PCT

(10) International Publication Number
WO 2005/051427 A1

- (51) International Patent Classification⁶: **A61K 47/00**
- (21) International Application Number:
PCT/US2004/037185
- (22) International Filing Date:
22 November 2004 (22.11.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
10/719,298 21 November 2003 (21.11.2003) US
- (71) Applicant (for all designated States except US): **CAD-BURY ADAMS USA LLC** [US/US]; 2711 Centerville Road, Suite 400, Wilmington, DE 19808 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **NAVROZ, Boghani** [US/US]; 17104 Topside Drive, Wharton, NJ 07885 (US). **GEBRESELASSIE, Petros** [SE/US]; 110A Pleasantview Drive, Piscataway, NJ 08854 (US).
- (74) Agent: **OBLON, Norman, F.**; Oblon, Spivak, McClelland, Maier & Neustadt, P.C., 1940 Duke Street, Alexandria, VA 22314 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
- with international search report
 - before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: A DELIVERY SYSTEM FOR ACTIVE COMPONENTS AS PART OF AN EDIBLE COMPOSITION HAVING PRE-SELECTED TENSILE STRENGTH

(57) Abstract: A delivery system for inclusion in an edible composition is formulated to have at least one active component encapsulated within an encapsulating material, whereby the delivery system has a tensile strength suitable for delivering the active component at a desired release rate.

WO 2005/051427 A1

Title of the Invention

A DELIVERY SYSTEM FOR ACTIVE COMPONENTS
AS PART OF AN EDIBLE COMPOSITION HAVING
PRESELECTED TENSILE STRENGTH

Field of the Invention

The present invention is generally directed to a delivery system for edible compositions in which a desired active component is encapsulated in a manner such that the tensile strength of the delivery system is within a desirable range to provide controlled release of the active component in a consistent manner over an extended period of time.

Background of the Invention

Encapsulating active components in edible compositions to prolong their release and/or to slow their degradation is known. Encapsulating materials used to coat such components include, for example, cellulose, cellulose derivatives, arabinogalactin, gum arabic, polyolefins, waxes, vinyl polymers, gelatin, zein and mixtures thereof. The encapsulating materials have been used to protect active components such as sweeteners, acids, flavorings, soluble dietary fibers, biologically active agents such as pharmaceutical compounds or medicinal drugs, breath freshening agents, and the like.

Attempts have been made to encapsulate active components such as sweeteners, particularly high intensity sweeteners to prevent against premature degradation, to enhance the uniformity of release, and to prolong release in a controlled manner. High intensity sweeteners generally have a sweetening intensity greater than sugar (sucrose) and a caloric value lower than that of sugar at equivalent sweetness levels. It is especially desirable to control the release of high intensity sweeteners in compositions since the high sweetness levels can easily overwhelm the consumer. Moreover, the controlled release of the sweetener provides desirable masking of unpleasant tasting materials. Because each high intensity sweetener is chemically and physically distinct, each is a challenge to use in an edible composition and each exhibits one or more shortcomings, which may be moderated by encapsulation.

For example, many high intensity sweeteners lose their sweetness intensity rapidly when used in edible compositions such as chewing gums and confections. Encapsulation can modulate and prolong release to provide a more desirable taste profile. Some high intensity sweeteners such as saccharin, stevioside, acesulfame-K, glycyrrhizin, and thaumatin have an associated bitter taste or off-note. Certain high intensity sweeteners are also unstable in the presence of certain chemicals including aldehydes and ketones, and sensitive to exposure to environmental conditions including moisture. Solid sucralose is known to turn dark during prolong storage upon exposure to heat and ambient air. Encapsulation can be used to isolate unstable compounds to prevent degradation and prolong shelf life.

Typically, the taste profile of a high intensity sweetener can be described as a rapid burst of sweetness. Usually, high intensity sweeteners reach their peak sweet taste rapidly, with the intensity of sweet taste rapidly declining soon thereafter. The initial rapid burst can be unpleasant to many consumers as the strong sweet taste tends to overpower the other flavors that may be present in the edible composition. The relatively rapid loss of sweetness can also result in a bitter aftertaste. For this reason, it is typically desirable to encapsulate high intensity sweeteners with an encapsulating material in order to modulate and prolong the release rate and to chemically stabilize and enhance the overall taste profile. The selection of a suitable encapsulating material (i.e., polyvinyl acetate) has usually been focused on the molecular weight of the encapsulating material with higher molecular weights generally associated with longer release times.

By way of example, U.S. Pat. No. 4,711,784 to Yang discloses a chewing gum composition containing a high molecular weight polyvinyl acetate blended with a hydrophobic plasticizer as an encapsulating material. The encapsulating material is used to encapsulate an active ingredient such as aspartame.

U.S. Pat. No. 4,816,265 to Cherukuri et al. discloses a sweetener delivery system, which uses a coating composed of an emulsifier and a polyvinyl acetate encapsulating material having a molecular weight of from about 2,000 to 14,000, optionally in the presence

of a wax. The coating is applied to sweeteners such as aspartame to effectuate sustained release of the sweetener.

U.S. Pat. No. 5,057,328 to Cherukuri et al. discloses a food acid delivery system for use in for example, chewing gums, having a food acid that is encapsulated in a matrix comprising an emulsifier and polyvinyl acetate in a specified molecular weight range.

U.S. Pat. No. 5,108,763 to Chau et al. discloses a sweetening agent delivery system having prolonged sweetener release. The system utilizes a high intensity sweetener encapsulated in polyvinyl acetate having a molecular weight in the range of from about 2,000 to 100,000. The system further includes the use of a plasticizing agent, a waxy material and an emulsifying agent.

U.S. Pat. No. 5,789,002 to Duggan et al. discloses a process for preparing sweeteners and acids as ingredients for chewing gum compositions. In particular, the Duggan et al. reference discloses encapsulating the sweetener or acid in a delivery system such as polyvinyl acetate.

U.S. Pat. Application No. 2002/0122842 filed by Seiestad et al. discloses food mixtures including chewing gums containing at least two acids encapsulated by a polyvinyl acetate matrix. The polyvinyl acetate has a molecular weight in the range of from about 20,000 to 120,000.

The prior art systems identified above prepare encapsulating materials by taking into account the selection of an encapsulating material (e.g. polyvinyl acetate) and its molecular weight.

Since polyvinyl acetate is the most common encapsulating material, the molecular weight of the material becomes a critical feature in the making of prior art delivery systems. Thus, the state of the art for encapsulating active components especially high intensity sweeteners essentially associates controlled release of the active component with the molecular weight of the encapsulating material. However, this approach is limited in that the

predictable modification of the controlled release of the active agent is made only through the modification of the molecular weight of the encapsulating material. There is no predictable modification based on the use of other encapsulating materials and/or additives that may be employed in the preparation of suitable delivery systems. Thus, there is no comprehensive approach to the production of a desirable delivery system that can provide a desirable release rate of an active component without engaging in a significant amount of trial and error experimentation.

It would therefore be a significant advance in the art to provide a process of producing delivery systems for the desirable release of an active component so that regardless of the type of the composition of the delivery system it will be suitable for the particular application (e.g., the controlled delivery of a high intensity sweetener).

Summary of the Invention

The present invention provides a new approach to the controlled release of an active component in edible compositions such as, for example, chewing gum and confectionery compositions. The active component(s) and materials used to encapsulate the same provide a delivery system(s) that enables exceptional control of the release of the active component over a wide range of delivery systems and takes into account the use of a range of encapsulating materials and additives that may be used to formulate the delivery system. The delivery system is formulated based on tensile strength as the prime factor in formulating a delivery system that can deliver a designated active component at a desirable release rate. The encapsulated active components are preserved until release is desirable and therefore protected against moisture, reactive compounds, pH changes and the like. When the active component is a sweetener, the delivery system is tailored to the sweetener to provide consistent sustained release, thus extending the time the sweetener is released to provide an edible composition which provides a long lasting desirable taste profile, increased salivation and overall enjoyment of the taste imparted therefrom without the disadvantage of prior art systems in which the sweetener may be released at less or more than a desirable rate.

The present invention is premised on the discovery that the tensile strength of the delivery system provides a desired controlled, extended release of an active component. As a result, a delivery system can be readily and easily formulated using a broad range of materials (e.g., encapsulating agents, active components, additives) with the desired characteristics to achieve a particular desirable release rate. The active components and materials used to encapsulate the same provide a delivery system that provides exceptional control of the release of the active component.

It has been found in accordance with the present invention that a delivery system for active components can be provided based on the tensile strength of the delivery system having a specific tensile strength when compared to a standard. This approach differs from those prior art systems that focus on one characteristic (molecular weight) of one of the materials (encapsulating material) used to produce the delivery system. In this manner, a delivery system is formulated to express a desired release profile by adjusting and modifying the tensile strength through the specific selection of the active component, the encapsulating material, the additives, the amount of the active component and the like which can be compared to at least one, typically a plurality of standard delivery systems each having a known release rate. Once a desired tensile strength is chosen, any delivery system which has the desired tensile strength may be used without being limited to a particular encapsulating material and its molecular weight. The formulation process can be extended to encapsulating materials which exhibit similar physical and chemical properties as the encapsulating material forming part of the standard delivery system.

As used herein, the term "tensile strength" means the maximum stress a material subjected to a stretching load can withstand without tearing. A standard method for measuring tensile strength of a given substance is defined by the American Society of Testing Materials in method number ASTM-D638.

In accordance with the present invention, the selection of a desired tensile strength within a desirable range enables the production of edible compositions using a range of materials including encapsulating materials without having to focus on a particular

encapsulating material and without being limited to modifying the release rate solely through the selection of a molecular weight for the encapsulating material.

Brief Description of the Drawings

The following drawings are illustrative of embodiments of the present invention and are not intended to limit the invention as encompassed by the claims forming part of the application.

Figure 1 is a graph comparing perceived sweetness intensity of three samples of gum over a 30 minute period in accordance with the present invention;

Figure 2 is a graph comparing perceived sweetness intensity of two samples of gum each containing different tensile strength delivery systems over a 30 minute period in accordance with the present invention;

Figure 3 is a graph comparing the percentage of aspartame retained over a period of time for two samples of gum containing different tensile strength delivery systems in accordance with the present invention; and

Figure 4 is a graph comparing perceived bitterness intensity of two gum samples each containing different tensile strength delivery systems in accordance with the present invention.

Detailed Description

In one aspect of the present invention, there is provided a delivery system for inclusion in an edible composition such as a chewing gum composition or confectionery composition having at least one active component encapsulated by an encapsulating material wherein the delivery system has a tensile strength of at least 6,500 psi, and typically ranging from about 6,500 psi to 200,000 psi.

In a further aspect of the present invention there is provided an edible composition such as a chewing gum composition or a confectionery composition comprising at least one edible composition-forming component and a delivery system comprising at least one active component encapsulated within an encapsulating material, the delivery system having a tensile strength of at least 6,500 psi.

In a still further aspect of the invention there is provided a method of preparing a target delivery system for an edible composition comprising combining at least one active component, at least one encapsulating material, and optionally at least one additive until a preselected tensile strength of the target delivery system is obtained based on comparison with the tensile strength of at least one sample delivery system having the same or similar active component and a known release rate of the active component.

There is also provided a method of preparing a target delivery system for an edible composition useful for delivering at least one active component at a desired release rate, said method comprising the step of encapsulating the at least one active component in an encapsulating material in a manner that provides the target delivery system with a tensile strength of at least 6,500 psi.

Still further there is provided a method of preparing a target delivery system for an edible composition useful for delivering at least one active component at a desired release rate, said method comprising encapsulating the at least one active component in an encapsulating material in a manner that provides the target delivery system with a target tensile strength associated with the desired release rate, enabling the delivery system to release the at least one active component from the edible composition at the desired release rate.

In addition, there is provided a method of preparing an edible composition containing a target delivery system useful for delivering at least one active component at a desired release rate, said method comprising encapsulating the at least one active component in an encapsulating material in a manner that provides the target delivery system with a target

tensile strength associated with the desired release rate enabling the delivery system to release the at least one active component from the edible composition at desired release rate, and adding the target delivery system to the edible composition.

There is also provided edible compositions containing the present delivery system. Although the one embodiment of the present invention relates to chewing gum compositions, confectionery compositions and beverages, the present invention can be utilized to produce a variety of edible compositions including, but not limited to, food products, foodstuffs, nutrient-containing compositions, pharmaceuticals, nutraceuticals, vitamins and other products that may be prepared for consumption by the consumer. Because the delivery system may be readily incorporated into an edible composition, the edible compositions which may benefit from and are encompassed by the present invention are wide ranging as indicated above.

The term "delivery system" as used herein is meant to encompass the encapsulating material and a single active component encapsulated therein as well as other additives used to form the delivery system as hereinafter described. It will be understood that the edible compositions of the present invention may contain a plurality of delivery systems with each delivery system containing a single active component.

The term "encapsulating material" is meant to encompass any one or more edible water insoluble materials capable of forming a solid coating or film as a protective barrier around the active component.

The present invention is directed generally to a delivery system as defined herein for use in edible compositions, which comprises an encapsulating material and an active component encapsulated by the encapsulating material. The delivery system of the present invention is formulated with a predetermined tensile strength sufficient to provide consistent controlled release of the active component over a preselected period of time such as an extended period of time. This period of time will vary depending on the type of product in which the delivery system is incorporated. One of skill in the art, based on the disclosure herein can adjust the delivery system to achieve the desired effect. An extended period of

time as used herein, relates to an increased release of the active ingredient from the delivery system for over a greater period of time than previously described systems and can be at least 15 minutes, including at least 20 minutes, at least 25 minutes, at least 30 minutes, as well as all values and ranges therebetween, for example, about 25 to 30 minutes or more. Furthermore, the delivery system of the present invention also provides a way to not only deliver active agents over a prolonged period of time but also maintain an increased intensity of the active ingredient over the extended period of time. For example, if the active ingredient is a flavor or sweetener. In one aspect of the invention, the amount of active agent released can vary during the extended period of time. For example, at an early stage of delivery the amount of active component released (based on the total amount present in the delivery system at that time) can be greater than the amount of active component released during subsequent or later periods (based on the total amount present in the delivery system at that time).

In one embodiment, the extended period of time results in retaining at least about 5% of the at least one active component after 30 minutes from the start of delivering the active component in the edible composition, such as the start of chewing a chewing gum composition, including at least about 10 %, 15%, 20 %, 25 %, 30 %, or more after 30 minutes. In another embodiment, the extended period of time results in retaining at least about 10% of the at least one active component after 20 minutes from the start of delivering the active component, including at least about 15%, 20 %, 25 %, 30 %, 40%, 50 % or more after 20 minutes. In another embodiment, the extended period of time results in retaining at least about 30% of the at least one active component after 15 minutes from the start of delivering the active component, including at least about 30 %, 40%, 50 %, 60 %, 70%, 75% or more after 15 minutes.

In another embodiment, using sweetener in chewing gum as an example, the extended period of time results in a perceived sweetness intensity during at least the entire period of time noted above, e.g., at least about 15 minutes, at least about 20 minutes, at least about 30 minutes, etcetera from the start of chewing the chewing gum composition.

The predetermined tensile strength is determined based, in part, on the active component and the desired release time of the same. The predetermined tensile strength may

be selected from a standard comprised of one or more delivery systems with each standard delivery system having a known release rate of the desired active component. The delivery system of the present invention further provides the active component with a protective barrier against moisture and other conditions such as pH changes, reactive compounds and the like, the presence of which can undesirably degrade the active component.

The delivery system facilitates the controlled release of the active component in a wide variety of edible compositions including chewing gum compositions, food products, confectionery compositions, pharmaceutical compositions, beverages, foodstuffs, nutrient-containing compositions, vitamins, nutraceuticals and the like.

The delivery system is developed in accordance with the present invention to have a desirable tensile strength which may be selected, depending in part on the active component and the release rate of the active component desired, from a standard of known delivery systems containing the active component at known release rates. The active components which may be incorporated as part of the delivery system may be selected from sweeteners including high intensity sweeteners, acids, flavorants, pharmaceuticals, therapeutic agents, vitamins, breath fresheners, cooling agents and other materials that would benefit by coating for protection, controlled release and/or for taste masking. The active components include nicotine useful for the treatment of addiction to tobacco products and caffeine typically found in coffee and/or cola beverages. In a particularly one form of the present invention, the active component is a sweetener, for example a high intensity sweetener such as neotame and aspartame.

It has been found in accordance with the present invention that a delivery system for delivering an active component can be formulated to ensure an effective sustained release of the active component based on the type and amount of the active component and desired release rate. For example, it may be desirable to effect the controlled release of a high intensity sweetener over a period of 25 to 30 minutes to ensure against a rapid burst of sweetness which may be offensive to some consumers. A shorter controlled release time may be desirable for other type of active components such as pharmaceuticals or therapeutic agents, which may be incorporated into the same edible composition by using separate

delivery systems for each active component. In accordance with the present invention, delivery systems may be formulated with a particular tensile strength associated with a range of release rates based on a standard. The standard may comprise a series of known delivery systems having tensile strengths over a range extending, for example, from low to high tensile strength values. Each of the delivery systems of the standard will be associated with a particular release rate or ranges of release rates. Thus, for example, a delivery system can be formulated with a relatively slow release rate by fabricating a delivering system having a relatively high tensile strength. Conversely, lower tensile strength compositions tend to exhibit relatively fast release rates. One factor of the present invention is that the tensile strength of the delivery system is directly associated with the release rate of the active component without direct regard for the type or molecular weight of the encapsulating material.

In one embodiment, the present invention includes the incorporation of a plurality of delivery systems to deliver a plurality of separate active components including active components which may be desirably released at distinctly different release rates.

For example, high intensity sweeteners may desirably be released over an extended period of time (e.g. 20 to 30 minutes) while some pharmaceuticals are desirably released over a significantly shorter period of time.

In certain embodiments of the present invention, the delivery system can be prepared such that the release of the at least one active agent is at specific rates relative to the time of delivery. For example, in one embodiment, the delivery system can be prepared such that the release of the at least one active agent is released at a rate of 80% over the course of 15 minutes, 90% over the course of 20 minutes, and/or a 95% over the course of 30 minutes. In another embodiment, the delivery system can be prepared such that the one or more active agents are released at a rate of 25 % over the course of 15 minutes, 50% over the course of 20 minutes and/or 75% over the course of 30 minutes.

In a one embodiment of the present invention, there is provided a method of selecting a target delivery system containing an active component for an edible composition. The

method generally includes preparing a targeted delivery system containing an active component, an encapsulating material and optional additives, with the targeted delivery system having a pre-selected tensile strength. The tensile strength of the targeted delivery system is pre-selected to provide a desirable release rate of the active component. This selection of the tensile strength is based on the tensile strengths of sample delivery systems having the same or similar active component and known release rates of the active component. In another embodiment of the invention, the method comprises the steps of (a) obtaining a plurality of sample delivery systems comprising an active component, at least one encapsulating material, and optional additives, wherein each of the delivery systems has a different tensile strength; (b) testing the sample delivery systems to determine the respective release rates of the active component; and (c) formulating a target delivery system containing the same active component with a tensile strength corresponding to a desired release rate of the active component based on the obtained sample delivery systems.

It will be understood that a plurality of delivery systems may be prepared in this manner each containing a different active component by utilizing a comparison with standard delivery systems containing such different active components.

The method of selecting at least one delivery system suitable for incorporation into an edible composition can begin by determining a desired release rate for an active component (i.e. a first active component). The determination of the desired release rate may be from known literature or technical references or by in vitro or in vivo testing. Once the desired release rate is determined, it is typical to determine the desired tensile strength (i.e. first tensile strength) for a delivery system (i.e. first delivery system) that can release the first active component at the desired release. Once the delivery system is obtained which can deliver the active component as required it is then selected for eventual inclusion in an edible composition.

The method described above may then be repeated for a second active component and for additional active components as described via the determination and selection of a suitable delivery system.

The present method can be used in connection with formulating the target delivery system using encapsulating materials having similar physical and chemical properties including the degree of water solubility, affinity for the active component, and the like as those used in the sample delivery systems.

Applicants have discovered that by maintaining the tensile strength of the delivery system within a preselected desirable range, the active component is released from the composition in a highly controlled and consistent manner irrespective of the particular type of encapsulating materials employed. By focusing on the tensile strength of the delivery system, the process for selecting and formulating suitable delivery systems is enhanced in a manner which effectively reduces the need for trial and error experimentation typically necessary in prior art systems. The present invention, for example, enables the formulation of a suitable target delivery system by focusing on a single variable (i.e., tensile strength) and therefore takes into account all components of the delivery system including encapsulating materials and any additives (e.g., fats and oils) that may be desirably added to the formulation and enables the delivery system when added to an edible composition to release the active component at a desirable release rate.

The desired tensile strength of the delivery system can be readily determined within a desired range. In one embodiment of the present invention, the tensile strength of the delivery system is at least 6,500 psi, including 7500, 10,000, 20,000, 30,000, 40,000, 50,000, 60,000, 70,000, 80,000, 90,000, 100,000, 125,000, 135,000, 150,000, 165,000, 175,000, 180,000, 195,000, 200,000 and all ranges and subranges there between, for example a tensile strength range of 6,500 to 200,000 psi. The formulation of a delivery system with a desirable tensile strength can be made from a variety of encapsulating materials and at least one additive which hereinafter are referred to as "at least one tensile strength modifying agent or modifier." The at least one additive may be used to formulate the delivery system by modifying the tensile strength of the delivery system, including tensile strength-lowering materials such as fats, emulsifiers, plasticizers (softeners), waxes, low molecular weight polymers, and the like, in addition to tensile strength increasing materials such as high molecular weight polymers. In addition, the tensile strength of the delivery system can also be fine tuned by combining different tensile strength modifiers to form the delivery system.

For example, the tensile strength of high molecular weight polymers such as polyvinyl acetate may be reduced when tensile strength lowering agents such as fats and/or oils are added.

In one embodiment of the present invention, at least one tensile strength modifying agent is present in the delivery system in an amount sufficient such that the release of the one or more active agents contained in the delivery system is released at a rate of 80% over the course of 15 minutes, 90% over the course of 20 minutes, and/or a 95% over the course of 30 minutes. In another embodiment, the at least one tensile strength modifying agent is present in the delivery system in an amount sufficient such that the one or more active agents are released at a rate of 25 % over the course of 15 minutes, 50% over the course of 20 minutes and/or 75% over the course of 30 minutes.

In another embodiment of the present invention, the at least one tensile strength modifying agent is present in the delivery system in an amount sufficient such that the tensile strength of the delivery system is at least about 6,500 psi, including 7500, 10,000, 20,000, 30,000, 40,000, 50,000, 60,000, 70,000, 80,000, 90,000, 100,000, 125,000, 135,000, 150,000, 165,000, 175,000, 180,000, 195,000, 200,000 and all ranges and subranges there between, for example a tensile strength range of 6,500 to 200,000 psi.

Examples of tensile strength modifiers or modifying agents include, but are not limited to, fats (e.g., hydrogenated or non-hydrogenated vegetable oils, animal fats), waxes (e.g., microcrystalline wax, bees wax), plasticizers/emulsifiers (e.g., mineral oil, fatty acids, mono- and diglycerides, triacetin, glycerin, acetylated monoglycerides, glycerol rosin monostearate esters), low and high molecular weight polymers (e.g., polypropylene glycol, polyethylene glycol, polyisobutylene, polyethylene, polyvinylacetate) and the like, and combinations thereof. Plasticizers may also be referred to as softeners.

Thus, by employing tensile strength modifiers, the overall tensile strength of the delivery system can be adjusted or altered in such a way that a preselected tensile strength is obtained for the corresponding desired release rate of the active component from an edible composition based on a comparison with a standard.

The delivery system of the present invention is typically in the form of a powder or granules. The particle size, generally, can vary and not have a significant effect on the function of the present invention. ~~however~~In one embodiment, the average particle size is desirably selected according to the desired rate of release and/or mouthfeel (i.e., grittiness) and the type of carrier incorporated in the edible composition. Thus, in certain embodiments of the present invention, the average particle size is from about 75 to about 600, including 100, 110, 140, 170, 200, 230, 260, 290, 320, 350, 370 and all values and ranges there between. As the values are an average one will appreciate within a given sample of powder or granules, there may be particles with sizes greater and/or less than the numerical values provided. In one embodiment of the invention, where the delivery system is incorporated into a chewing gum the particle size can be less than 600 microns.

Except as otherwise noted, the amount of the ingredients incorporated into the compositions according to the present invention is designated as % by weight based on the total weight of the composition.

The delivery systems of the present invention produce controlled release of the active components as desired through the use of a preselected tensile strength when matched with a desirable release rate selected according to the type of the active components to be encapsulated, the encapsulating material used, the additives incorporated, the desired rate of release of the active component, and the like. The materials used to encapsulate the active component are generally selected from edible water insoluble materials capable of forming a strong matrix, solid coating or film as a protective barrier around the active component. The encapsulating material is chosen in a manner consistent with the tensile strength of the delivery system which can be at least 6,500 psi, including 7500, 10,000, 20,000, 30,000, 40,000, 50,000, 60,000, 70,000, 80,000, 90,000, 100,000, 125,000, 135,000, 150,000, 165,000, 175,000, 180,000, 195,000, 200,000 and all ranges and subranges there between, for example a tensile strength range of 6,500 to 200,000 psi. Such encapsulating materials may be selected from polyvinyl acetate, polyethylene, crosslinked polyvinyl pyrrolidone, polymethylmethacrylate, polylactidacid, polyhydroxyalkanoates, ethylcellulose, polyvinyl

acetatephthalate, polyethylene glycol esters, methacrylicacid-co-methylmethacrylate, and the like, and combinations thereof.

The encapsulating material may be present in amounts of from about 0.2% to 10% by weight based on the total weight of the edible composition, including 0.3, 0.5, 0.7, 0.9, 1.0, 1.25, 1.4, 1.7, 1.9, 2.2, 2.45, 2.75, 3.0, 3.5, 4.0, 4.25, 4.8, 5.0, 5.5, 6.0, 6.5, 7.0, 7.25, 7.75, 8.0, 8.3, 8.7, 9.0, 9.25, 9.5, 9.8 and all values and ranges there between, for example, from 1% to 5% by weight. The amount of the encapsulating material will, of course, depend in part on the amount of the active component which must be encapsulated. The amount of the encapsulating material with respect to the weight of the delivery system, is from about 30% to 99%, including 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 95, 97 and all values and ranges there between, for example, from about 60% to 90% by weight.

The tensile strength of the delivery system may be selected from relatively high tensile strengths when a relatively slow rate of release is desired and relatively lower tensile strengths when a faster rate of release is desired. Thus, when employing a tensile strength of 50,000 for a delivery system, the release rate of the active component, will generally be lower than the release rate of the active component in a delivery system having a tensile strength of 10,000 psi regardless of the type of encapsulating material (e.g. polyvinyl acetate) chosen.

In a one embodiment of the present invention, the encapsulating material is polyvinyl acetate. A representative example of a polyvinyl acetate product suitable for use as an encapsulating material in the present invention is Vinnapas® B100 sold by Wacker Polymer Systems of Adrian, Michigan. A delivery system utilizing polyvinyl acetate may be prepared by melting a sufficient amount of polyvinyl acetate at a temperature of about 65° to 120°C for a short period of time, e.g., 5 minutes. The melt temperature will depend on the type and tensile strength of the polyvinyl acetate encapsulating material where higher tensile strength materials will generally melt at higher temperatures. Once the encapsulating material is melted, a suitable amount of the active component (e.g., high intensity sweetener such as aspartame) is added and blended into the molten mass thoroughly for an additional short period of mixing. The resulting mixture is a semi-solid mass, which is then cooled (e.g., at 0°C) to obtain a solid, and then ground to a U.S. Standard sieve size of from about 30 to 200

(600 to 75 microns). The tensile strength of the resulting delivery system can readily be tested according to ASTM-D638.

The selection of a suitable encapsulating material will also depend in part on the type and amount of the active component and the presence of other additives or ingredients. Plasticizers or softeners as well as fats and oils, for example, act as "tensile strength modifying agents" and may be incorporated into the delivery system and particularly into the encapsulating material to modify the tensile strength of the resulting delivery system. The above mentioned additives may be added to the encapsulating material during the molten state. The amount of additives used in the delivery system of the present invention will of course vary according to the desired tensile strength but will typically range up to 40% by weight based on the total weight of the delivery system.

In formulating the delivery system to have a predetermined tensile strength, the active component can be entirely encapsulated within the encapsulating material or incompletely encapsulated within the encapsulating provided the resulting tensile strength of the delivery system meets the criteria set forth hereinabove. The incomplete encapsulation can be accomplished by modifying and/or adjusting the manufacturing process to get partial coverage of the active component.

The presence of fats and oils as an additive has been found to have two effects on the delivery system. The first effect is observed at lower concentrations, i.e. up to 5% by weight, including up to 4.7, up to 4.5, up to 4.25, up to 4.0, up to 3.5, up to 3.0, up to 2.5, up to 2.25, up to 2.0, up to 1.75, up to 1.5, up to 1.0 and all values and ranges therebetween, wherein the fats and/or oils either maintain or increase the tensile strength of the delivery system. At higher concentrations (i.e., typically above 5% by weight), the fats and/or oils tend to reduce the tensile strength of the delivery system. Even with such unusual or non-linear effects on the tensile strength of the delivery system, a suitable delivery system with the desired release of the active component may be readily formulated in accordance with the present invention because the targeted delivery system is prepared based on sample delivery systems having known release rates for the active component.

Although the present description made herein relates to sweeteners, it will be understood that the effect of tensile strength on the delivery system will be similar regardless of the active component.

The sweetening agents used may be selected from a wide range of materials including water-soluble sweeteners, water-soluble artificial sweeteners, water-soluble sweeteners derived from naturally occurring water-soluble sweeteners, dipeptide based sweeteners, and protein based sweeteners, including mixtures thereof. Without being limited to particular sweeteners, representative categories and examples include:

(a) water-soluble sweetening agents such as dihydrochalcones, monellin, steviosides, glycyrrhizin, dihydroflavenol, and sugar alcohols such as sorbitol, mannitol, maltitol, and L-aminodicarboxylic acid aminoalkenoic acid ester amides, such as those disclosed in U.S. Pat. No. 4,619,834, which disclosure is incorporated herein by reference, and mixtures thereof;

(b) water-soluble artificial sweeteners such as soluble saccharin salts, i.e., sodium or calcium saccharin salts, cyclamate salts, acesulfame salts, such as the sodium, ammonium or calcium salt of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide, the potassium salt of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide (Acesulfame-K), the free acid form of saccharin, and mixtures thereof;

(c) dipeptide based sweeteners, such as L-aspartic acid derived sweeteners, such as L-aspartyl-L-phenylalanine methyl ester (Aspartame) and materials described in U.S. Pat. No. 3,492,131, L-alphaaspartyl-N-(2,2,4,4-tetramethyl-3-thietanyl)-D-alaninamide hydrate (Alitame), methyl esters of L-aspartyl-L-phenylglycerine and L-aspartyl-L-2,5-dihydrophenyl-glycine, L-aspartyl-2,5-dihydro-L-phenylalanine; L-aspartyl-L-(1-cyclohexen)-alanine, neotame, and mixtures thereof;

(d) water-soluble sweeteners derived from naturally occurring water-soluble sweeteners, such as steviosides, chlorinated derivatives of ordinary sugar (sucrose), e.g., chlorodeoxysugar derivatives such as derivatives of chlorodeoxysucrose or chlorodeoxygalactosucrose, known, for example, under the product designation of Sucralose; examples of chlorodeoxysucrose and chlorodeoxygalactosucrose derivatives include but are not limited to: 1-chloro-1'-

deoxysucrose; 4-chloro-4-deoxy-alpha-D-galactopyranosyl-alpha-D-fructofuranoside, or 4-chloro-4-deoxygalactosucrose; 4-chloro-4-deoxy-alpha-D-galactopyranosyl-1-chloro-1-deoxy-beta-D-fructo-furanoside, or 4,1'-dichloro-4,1'-dideoxygalactosucrose; 1',6'-dichloro 1',6'-dideoxysucrose; 4-chloro-4-deoxy-alpha-D-galactopyranosyl-1,6-dichloro-1,6-dideoxy-beta-D- fructofuranoside, or 4,1',6'-trichloro-4,1',6'-trideoxygalactosucrose; 4,6-dichloro-4,6-dideoxy-alpha-D-galactopyranosyl-6-chloro-6-deoxy-beta-D- fructofuranoside, or 4,6,6'-trichloro-4,6,6'-trideoxygalactosucrose; 6,1',6'-trichloro-6,1',6'-trideoxysucrose; 4,6-dichloro-4,6-dideoxy-alpha-D-galacto-pyranosyl-1,6-dichloro-1,6-dideox y-beta-D-fructofuranoside, or

4,6,1',6'-tetrachloro-4,6,1',6'-tetraideoxygalacto-sucrose; and 4,6,1',6'-tetraideoxy-sucrose, and mixtures thereof; and

(e) protein based sweeteners such as thaumaococcus danielli (Thaumatococcus I and II), talin.

The intense sweetening agents may be used in many distinct physical forms well-known in the art to provide an initial burst of sweetness and/or a prolonged sensation of sweetness. Without being limited thereto, such physical forms include free forms, such as spray dried, powdered, beaded forms, encapsulated forms, and mixtures thereof. In one embodiment, the sweetener is a high intensity sweetener such as aspartame, sucralose, and acesulfame potassium (Ace-K).

The active component (e.g., sweetener), which is part of the delivery system, may be used in amounts necessary to impart the desired effect associated with use of the active component (e.g., sweetness). With respect to their presence in the delivery system, the active components may be present in amounts of from about 1% to 70% by weight based on the total weight of the delivery system, including 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65% by weight, and all values and ranges there between, for example, from about 10% to 40% by weight based on the total weight of the delivery system. For typical edible compositions including chewing gum compositions, confectionery compositions and beverage compositions, the sweeteners may be present in amounts of from about 0.1% to 6% by weight based on the total weight of the edible composition, including 0.5, 1, 2, 3, 4, 5 % by weight and all values and subranges there between, for example, 0.5% to 3% by weight.

The active component especially when the active component is a sweetener may also be present in the edible composition in free form depending on the release profile desired.

In another aspect of the present invention, there is provided edible compositions which comprise the present delivery system and a carrier in an amount appropriate to accommodate the delivery system. The term "carrier" as used herein refers to an orally acceptable vehicle such as the soluble and insoluble components of a chewing gum composition capable of being mixed with the delivery system, and which will not cause harm to warm-blooded animals including humans. The carriers further include those components of the composition that are capable of being commingled without significant interaction with the delivery system.

In a one embodiment of the present invention, the edible composition is a chewing gum composition having prolonged release (e.g., typically at least 15 minutes) of the active component. The chewing gum composition comprises a chewing gum base and the delivery system of the present invention that comprises an encapsulating material and at least one encapsulated active component such as, for example, a sweetener or a flavorant. The delivery system is present in amounts from about 0.2% to 10% by weight based on the total weight of the chewing gum composition, including 0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 9.0 % by weight including all values and subranges there between, for example, from about 1% to 5% by weight.

The present invention may be incorporated with a variety of processes for preparing chewing gum compositions as known in the art. Such chewing gum compositions may be and include a variety of different formulations that are typically used to make chewing gum products. Typically, a chewing gum composition contains a chewable gum base portion, which is essentially free of water and is water insoluble and a water soluble bulk portion.

The water soluble portion is generally released from the gum base portion over a period of time during chewing. The gum base portion is retained in the mouth throughout the chewing. The water insoluble gum base generally comprises elastomers, elastomer solvents, plasticizers, waxes, emulsifiers, and inorganic fillers. Plastic polymers such as polyvinyl

acetate, which behave somewhat as plasticizers, are also included. Other plastic polymers that may be used include polyvinyl laurate, crosslinked polyvinyl pyrrolidone and polyhydroxy alkanoates.

The elastomers may constitute from about 5% to 95% by weight of the gum base. In another embodiment, the elastomers may constitute from about 10% to 70% by weight of the gum base and in another embodiment, 15% to 45% by weight of the gum base. Examples of elastomers include synthetic elastomers such as polyisobutylene, polybutylene, isobutylene-isoprene co-polymers, styrene-butadiene co-polymers, polyvinyl acetate and the like. Elastomers may also include natural elastomers such as natural rubber as well as natural gums such as jelutong, lechi caspi, perillo, massaranduba balata, chicle, gutta hang kang or combinations thereof. Other elastomers are known to those of ordinary skill in the art.

Elastomer plasticizers modify the finished gum firmness when used in the gum base. Elastomer plasticizers are typically present in an amount up to 75% by weight of the gum base. In another embodiment, the elastomer plasticizers are present in an amount of from about 5% to 45% by weight of the gum base and in another embodiment from about 10% to 30% by weight of gum base. Examples of elastomer plasticizers include natural rosin esters such as glycerol ester of partially hydrogenated rosin, glycerol ester of tall oil rosin, pentaerythritol esters of partially hydrogenated rosin, methyl and partially hydrogenated methyl esters of rosin, and the like. Synthetic elastomer plasticizers such as terpene resins may also be employed in gum base composition.

Waxes include synthetic and naturally occurring waxes such as polyethylene, bees wax, carnauba and the like. Petroleum waxes such a paraffin may also be used. The waxes may be present in the amount up to 30% by weight of the gum base. Waxes aid in the curing of the finished gum and help improve the release of flavor and may further extend the shelf life of the product.

Elastomer solvents are often resins such as terpene resins. Plasticizers, sometimes referred to as softeners, are typically fats and oils, including tallow, hydrogenated vegetable oils, and cocoa butter.

Gum base typically also includes a filler component. The filler component modifies the texture of the gum base and aid processing. Examples of such fillers include magnesium and aluminum silicates, clay, alumina, talc, titanium oxide, cellulose polymers, and the like. Fillers are typically present in the amount of from 1% to 60% by weight.

Emulsifiers, which sometimes also have plasticizing properties, include glycerol monostearate, lecithin, and glycerol triacetate. Further, gum bases may also contain optional ingredients such as antioxidants, colors, and flavors.

The insoluble gum base may be present in the amount of from about 5% to 95% by weight of the chewing gum. In one embodiment, the insoluble gum base may present in the amount of from about 10% to 50% by weight of the gum base, and in another embodiment from about 20% to 40% by weight of the gum base.

Softeners are added to the chewing gum in order to optimize the chewability and mouth feel of the gum. Softeners, also known in the art as plasticizers or plasticizing agents, is generally present in amounts from about 0.5% to 15% by weight based on the total weight of the chewing gum composition. Softeners contemplated by the present invention include, for example, lecithin. Further, aqueous sweetener solutions such as those containing sorbitol, hydrogenated starch hydrolysate, corn syrup, and combinations thereof may be used as softeners and binding agents in the gum.

The chewing gum compositions of the present invention may be coated or uncoated and be in the form of slabs, sticks, pellets, balls and the like. The composition of the different forms of the chewing gum compositions will be similar but may vary with regard to the ratio of the ingredients. For example, coated gum compositions may contain a lower percentage of softeners. Pellets and balls have a small chewing gum core, which is then coated with either a sugar solution or a sugarless solution to create a hard shell. Slabs and sticks are usually formulated to be softer in texture than the chewing gum core.

In accordance with one aspect of the chewing gum composition of the present invention, the delivery system is added during the manufacture of the chewing gum composition. In another aspect of the present invention, the delivery system is added as one of the last steps, for example, the last step in the formation of the chewing gum composition. Applicants have determined that this process modification incorporates the delivery system into the gum composition without materially binding the delivery system therein such as may occur if the delivery system is mixed directly with the gum base. Thus, the delivery system, while only loosely contained within the gum composition can more effectively release the active component therefrom during a typical chewing operation. Thus, a material portion of the delivery system is free of the gum base and the corresponding ingredients of the chewing gum.

Coating techniques for applying a coating for a chewing gum composition such as pan and spray coating are well known. In one embodiment, coating with solutions adapted to build a hard candy layer can be employed. Both sugar and sugar alcohols may be used for this purpose together with high intensity sweeteners, colorants, flavorants and binders.

Other components may be added in minor amounts to the coating syrup and include moisture absorbing compounds, anti-adherent compounds, dispersing agents and film forming agents. The moisture absorbing compounds suitable for use in the coating syrups include mannitol or dicalcium phosphate. Examples of useful anti-adherent compounds, which may also function as a filler, include talc, magnesium trisilicate and calcium carbonate. These ingredients may be employed in amounts of from about 0.5% to 5% by weight of the syrup. Examples of dispersing agents, which may be employed in the coating syrup, include titanium dioxide, talc or other anti-adherent compounds as set forth above.

The coating syrup is usually heated and a portion thereof deposited on the cores. Usually a single deposition of the coating syrup is not sufficient to provide the desired amount or thickness of coating and second, third or more coats of the coating syrup may be applied to build up the weight and thickness of the coating to desired levels with layers allowed to dry in-between coats.

A method of preparing the chewing gum composition of the present invention is provided by sequentially adding the various chewing gum ingredients including the delivery system of the present invention to any commercially available mixer known in the art. After the ingredients have been thoroughly mixed, the gum base is discharged from the mixer and shaped into the desired form such as by rolling into sheets and cutting into sticks, extruding into chunks, or casing into pellets.

Generally, the ingredients are mixed by first melting the gum base and adding it to the running mixer. The base may also be melted into the mixer itself. Colors or emulsifiers may also be added at this time. A softener may be added to the mixer at this time, along with syrup and a portion of the bulking agent. Further parts of the bulking agent are then added to the mixer. Flavorants are typically added with the final portion of the bulking agent. Finally, the delivery system exhibiting a predetermined tensile strength is added to the resulting mixture. Other optional ingredients are added in the batch in a typical fashion, well known to those of ordinary skill in the art.

The entire mixing procedure typically takes from five to fifteen minutes, but longer mixing times may be required. Those skilled in the art will recognize that many variations of the above-described procedure may be follows.

After the ingredients are mixed, the gum mass may be formed into a variety of shapes and products. For example, the ingredients may be formed into pellets or balls and used as cores to make a coated chewing gum product. However, any type of chewing gum product can be utilized with the present invention.

If a coated product is desired, the coating may contain ingredients such as flavorants, artificial sweeteners, dispersing agents, coloring agents, film formers and binding agents. Flavorants contemplated by the present invention, include those commonly known in the art such as essential oils, synthetic flavors, or mixtures thereof, including but are not limited to, oils derived from plants and fruits such as citrus oils, fruit essences, peppermint oil, spearmint oil, other mint oils, clove oil, oil of wintergreen, anise and the like. The flavorants may also be added to the coating syrup in an amount such that the coating may be present in

amounts of from about 0.2% to 1.2% by weight flavoring agent. In another embodiment, the coating may be present in amounts, and more preferably from about 0.7% to 1.0% by weight flavoring agent.

Dispersing agents are often added to syrup coatings for the purpose of whitening and tack reduction. Dispersing agents contemplated by the present invention to be employed in the coating syrup include titanium dioxide, talc, or any other anti-stick compound. The dispersing agent may be added to the coating syrup in an amount such that the coating contains from about 0.1% to 1.0%, including 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9 and all values and ranges there between, for example, from about 0.3% to 0.6% by weight of the agent.

Coloring agents may be added directly to the coating syrup in dye or lake form. Coloring agents contemplated by the present invention include food quality dyes. Film formers may be added to the coating syrup include methylcellulose, carboxymethyl cellulose, ethyl cellulose, hydroxyethyl cellulose, and the like or combinations thereof. Binding agents may be added either as an initial coating on the chewing gum center or may be added directly to the coating syrup. Binding agents contemplated by the present invention include gum arabic, gum talha, gelatin, vegetable gums, and the like. The binding agents, when added to the coating syrup, are typically added in amounts from about 0.5% to 10% by weight.

The present invention further encompasses confectionery compositions containing the delivery system of the present invention. Confectionery compositions include, for example, compressed tablets such as mints, hard boiled candies, chocolates, chocolate containing products, nutrient bars, nougats, gels, centerfill confections, fondants, panning goods, consumable thin films and other compositions falling within the generally accepted definition of confectionery compositions.

Confectionery compositions in the form of pressed tablets such as mints may generally be made by combining finely sifted sugar or sugar substitute, flavoring agent (e.g. peppermint flavor) bulking agent such as gum arabic, and an optional coloring agent. The flavoring agent, bulking agent are combined and then gradually the sugar or sugar substitute are added along with a coloring agent if needed.

The product is then granulated by passing through a sieve of desired mesh size (e.g. 12 mesh) and then dried typically at temperatures of from about 55°C to 60°C. The resulting powder is fed into a tableting machine fitted with a large size punch and the resulting pellets are broken into granules and then pressed.

High boiled candies typically contain sugar or sugar substitute, glucose, water, flavoring agent and optional coloring agent. The sugar is dissolved in the water and glucose is then added. The mixture is brought to a boil. The resulting liquid to which may previously have been added a coloring agent is poured onto an oiled slab and cooled. The flavoring agent are then added and kneaded into the cooled mass. The resulting mixture is then fed to a drop roller assembly known in the art to form the final hard candy shape.

A nougat composition typically includes two principal components, a high boiled candy and a frappe. By way of example, egg albumen or substitute thereof is combined with water and whisked to form a light foam. Sugar and glucose are added to water and boiled typically at temperatures of from about 130°C to 140°C and the resulting boiled product is poured into a mixing machine and beat until creamy.

The beaten albumen and flavoring agent are combined with the creamy product and the combination is thereafter thoroughly mixed.

Further details regarding the preparation of confectionery compositions can be found in Skuse's Complete Confectioner (13th Edition) (1957) including pp. 41-71, 133-144, and 255-262; and Sugar Confectionery Manufacture (2nd Edition) (1995), E.B. Jackson, Editor, pp. 129-168, 169-188, 189-216, 218-234, and 236-258 each of which is incorporated herein by reference.

EXAMPLE 1

The following study shows the effect of the presence of oil or fats on the overall tensile strength of one embodiment of the delivery system of the present invention. The rate of release of the active component (i.e., aspartame) is affected by the variation in tensile strength such that the release rate of the higher tensile strength delivery system is generally slower than the release rate of lower tensile strength formulations. When relatively large amounts of oil or fat are used, the tensile strength of the delivery system is generally lowered which increases the release rate of the active component. Conversely, reduced amounts of fats or oils are employed typically for higher tensile strength delivery systems exhibiting lower release rates.

Experimental Procedure

Preparation of the delivery systems

Four delivery systems for delivering a high intensity sweetener (i.e., aspartame) containing varying amounts of polyvinyl acetate, and oils or fat were prepared in accordance with the formulations shown in Table 1.

Table 1

| <u>Ingredient</u> | <u>Delivery</u> <u>System 1</u> (20% Fat) | <u>Delivery</u> <u>System 2</u> (10% Fat) | <u>Delivery</u> <u>System 3</u> (0% Fat) | <u>Delivery</u> <u>System 4</u> (5% Fat) |
|-------------------------------|---|---|--|--|
| Polyvinyl acetate B100 | 50% | 60% | 70% | 65 |
| Hydrogenated Oil | 15% | 7.5% | 0% | 3.5 |
| Glycerol Monostearate | 5% | 2.5% | 0% | 1.5 |
| Aspartame | 30% | 30% | 30% | 30% |
| Tensile Strength (psi) | 10,829 | 24,833 | 22,761 | 42,900 |

Polyvinyl acetate was melted at a temperature of about 110°C in a continuous extruder. The hydrogenated oil and glycerol monostearate (fat) were added to the molten polyvinyl acetate. Aspartame was then added to the resulting mixture and mixed under high shear to completely disperse the ingredients. The resulting extrudate was cooled and then sized to a particle size of less than 420 microns to produce the corresponding delivery system containing the encapsulated high intensity sweetener aspartame as the active component. The tensile strength of each of the final delivery systems was measured in accordance with ASTM Standard D638-02a and is shown in Table 1.

As indicated in Table 1, the addition of fats and oils exhibits two effects on the tensile strength of the delivery system when a portion of the encapsulating material (polyvinyl acetate) is replaced by the fats and oils. As shown by a comparison of delivery system no. 3 to delivery system no. 4, there is a sharp increase in tensile strength when 5% by weight of polyvinyl acetate is replaced by a corresponding amounts of fats and oils. When the replacement is 10% by weight the tensile strength drops significantly but remains above the level of the fat and oil free delivery system (delivery system no. 1). When fats and oils are used in relatively large amounts (i.e., 20% by weight), the delivery system tends to exhibit a much lower tensile strength as compared to delivery system no. 3.

Preparation of the chewing gums

Three sample chewing gum compositions were prepared using the ingredients listed in Table 2 and incorporating delivery system nos. 1 through 3 as shown in Table 1.

Table 2

| <u>Ingredient</u> | <u>Chewing Gum 1</u> | <u>Chewing Gum 2</u> | <u>Chewing Gum 3</u> |
|-------------------|----------------------|----------------------|----------------------|
| Gum base | 39.0 | 39.0 | 39.0 |
| Sorbitol | 42.8 | 42.8 | 42.8 |
| Mannitol | 9.0 | 9.0 | 9.0 |
| Flavor | 4.67 | 4.67 | 4.67 |
| Glycerin | 1.5 | 1.5 | 1.5 |
| Lecithin | 0.2 | 0.2 | 0.2 |
| Delivery System 1 | 2.83 | - | - |
| Delivery System 2 | - | 2.83 | - |
| Delivery System 3 | - | - | 2.83 |

The chewing gum composition was prepared as follows. The gum base was melted at a suitable temperature in a mixer. The remaining ingredients were then added to the melted gum base and mixed until the ingredients were completely dispersed. The resulting chewing gum composition was sized and conditioned for about 1 week and evaluated using a pool of human subjects. Each of the human subjects were asked to sample the chewing gum compositions by chewing each of the samples listed in Table 2 and rating the sweetness intensity of each sample at 10 minute intervals over a 30 minute time period. The resulting data is shown in Figure 1.

Results

As shown in Figure 1, Gum 3 prepared with fat and oil free delivery system no. 3 provided extended sweetener release with higher sweetener intensity measured at each of the intervals as compared to Gums 1 and 2 each of which contained a delivery system with some level of oil and fat. Gum 1 prepared from delivery system no. 1, which exhibited the lowest tensile strength due in part to its higher oil and fat content, had a relatively short duration of

sweetener release and exhibited the lowest sweetener intensity subsequent to the initial release as measured at each of the 10 minute intervals.

It will be understood that each of the chewing gum compositions prepared in accordance with Example 1 could readily be modified to include one or more additional delivery systems each containing a different active component.

EXAMPLE 2

The following study examined the relationship between tensile strength of the delivery system and the release rate of the encapsulated active component. The presence of fats or oils were varied to modify the tensile strength of the delivery system, thereby allowing the release rate of the encapsulated active component to be adjusted as desired.

Experimental Procedure

Preparation of the delivery systems

Four delivery systems were prepared using the ingredients listed in Table 3.

Table 3

| <u>Ingredient</u> | <u>Delivery System 5</u> | <u>Delivery System 4</u> | <u>Delivery System 6</u> | <u>Delivery System 7</u> |
|---|------------------------------|------------------------------|------------------------------|------------------------------|
| Polyvinyl acetate (High Tensile Strength) | | 65% | | 65% |
| Polyvinyl acetate (Low Tensile Strength) | 63% | | 63% | |
| Hydrogenated Oil | 15% | 3.5% | 15% | 3.5% |
| Glycerol Monostearate | 5% | 1.5% | 5% | 1.5% |
| Aspartame | 17% | 30% | | |
| Acesulfame-K | | | 17% | 30% |
| | | | | |
| Tensile Strength (psi) | 6,500 | 42,900 | * | ** |

* not measured but believed to be similar to delivery system no. 5

**not measured but believed to be similar to delivery system no. 4

The above delivery systems (i.e., delivery system nos. 4 to 7) were prepared in the following manner. The polyvinyl acetate encapsulating materials were melted at a temperature of about 110°C in a continuous extruder. Hydrogenated oil and glycerol monostearate were added to the molten encapsulating materials. The sweetener was then added to the resulting mixture. The mixture was thoroughly mixed under high shear to completely disperse the ingredients to yield an extrudate. The mixed extrudate was thereafter allowed to cool and comminuted to yield particles of the respective delivery systems having a particle size of about less than 600 microns. The delivery systems were each formulated to exhibit a specific tensile strength, in part based on the amount and strength of the polyvinyl acetate and the amount of the fats and oils and other components. The tensile strength of each of delivery system nos. 4 through 7 is listed in Table 3.

Preparation of chewing gum samples

Two test samples of chewing gum compositions referred to herein as Gums 4 and 5 were prepared and formulated with the ingredients listed in Table 4 below. Gum 4 was formulated with a combination of delivery system nos. 5 and 6 shown in Table 3 in the specified amounts to yield a chewing gum having a relatively low tensile strength delivery system. Gum 5 was formulated with a combination of delivery system nos. 4 and 7 in the specified amounts to yield a chewing gum having a relatively high tensile strength delivery system.

Table 4

| <u>Ingredient</u> | <u>Chewing Gum 4</u> | <u>Chewing Gum 5</u> |
|-------------------|----------------------|----------------------|
| Gum base | 39.0% | 39.0% |
| Sorbitol | 42.5% | 44.3% |
| Mannitol | 9.0% | 9.0% |
| Flavor | 3.67% | 3.67% |
| Glycerin | 1.5% | 1.5% |
| Lecithin | 0.2% | 0.2% |
| Delivery System 5 | 2.94% | - |
| Delivery System 6 | 1.26% | - |
| Delivery System 4 | - | 1.63% |
| Delivery System 7 | - | 0.7% |

The above test sample chewing gums were each prepared in the following manner. The gum base was melted in a mixer. The remaining ingredients were added to the melted gum base. The melted gum base was mixed to completely disperse the ingredients. The resulting chewing gum was allowed to cool. The cooled chewing gum was sized and conditioned for about a week.

It will be understood that each of the chewing gum compositions prepared in accordance with Example 2 could readily be modified to include one or more additional delivery systems each containing a different active component.

Descriptive Panel Evaluation

Sweetness and Bitterness Intensity Analysis

A pool of human subjects was assembled to taste and rate the sweetness intensity of the chewing gum test samples over time. Each of the human subjects were asked to sample by chewing the test sample gums 4 and 5 over a 30 minute period. At each 5-minute interval, the human subjects were asked to rate the perceived sweetness intensity of the chewing gum sampled on a scale of 1 to 10. The results are shown in Figure 2.

Further to measuring sweetness intensity as perceived by the humans subjects during the chewing, the human subjects were also asked to rate the perceived bitterness intensity of the chewing on a similar scale of 1 to 10. The results are shown in Figure 4.

Residual Sweetener Analysis

The chewing gums chewed by the human subjects were also subjected to chemical analysis at 5-minute intervals to measure the amount of the residual sweetener remaining in the gum bolus. Every 5 minutes over the 30-minute period, the bolus of the chewing gum was retrieved from each of the human subjects and tested by high-performance liquid chromatography (HPLC). The results are shown in Figure 3.

Results

Descriptive panel results:

As shown in Figure 2, the perceived sweetness intensity of Gum 4 having the lower tensile strength delivery system decreased significantly more rapidly than Gum 5 having the higher tensile strength delivery system over the 30 minute period. From the data presented in Figure 2, high tensile strength delivery systems tends to extend the duration of sweetener release from the chewing gum.

As shown in Figure 4, the results indicate that Gum 5 possessing the higher tensile strength delivery system exhibited an initial perceived bitterness intensity that was relatively higher than Gum 4 (i.e., lower tensile strength delivery system). However, over the course of the next 20 minutes, the perceived bitterness in Gum 5 (higher tensile strength) decreased over time, while the perceived bitterness (lower tensile strength) increased over time and remained above the bitter intensity of Gum 5. The results show that the release rate of the sweetener affects the perception of the inherent bitter flavor that may be normally present in chewing gum compositions. The slower release rate of the sweetener in Gum 5 (higher tensile strength) extended the duration of the taste masking over the course of the 25 minutes, thus reducing the perception of bitter taste as compared to Gum 4 (lower tensile strength).

Human Chew-out / Residual Aspartame

As shown in Figure 3, Gum 4 having a delivery system with a relatively lower tensile strength exhibited a higher rate of sweetener release than Gum 5 having a delivery system with a relatively higher tensile strength over the 30 minute period. Accordingly, by increasing the tensile strength of the delivery system, a lower rate of release of the sweetener can thereby be achieved. Conversely, reducing the tensile strength of the delivery system increases the rate of release of the sweetener. Chewing Gum 4 with the relatively lower tensile strength delivery system further showed a lower residual amount aspartame in the chewed cuds as compared to Gum 5 with the relatively higher tensile strength delivery system. Thus, the data shows that higher tensile strength delivery systems generally provide a slower rate of release of the sweeteners. The results shown in Figure 3 are consistent with the results shown in Figure 2 in that faster release of the sweetener results in less sweetener retained in the gum over time.

The forgoing discussion discloses and describes merely exemplary embodiments of the present invention. One skilled in the art will readily recognize from such discussion, and from the accompanying claims, that various changes, modifications, and variations can be made therein without departing from the spirit and scope of the invention as defined in the following claims.

What is Claimed is:

1. A delivery system comprising at least one active component encapsulated within an encapsulating material, the delivery system having a tensile strength of at least 6,500 psi.
2. The delivery system of claim 1 wherein the tensile strength of the delivery system is from about 6,500 psi to 200,000 psi.
3. The delivery system of claim 1 wherein the edible composition is selected from the group consisting of a food product, a pharmaceutical composition, a foodstuff, a nutrient-containing composition, a vitamin, a nutraceuticals, and combinations thereof.
4. The delivery system of claim 1 wherein the edible composition is selected from a food product, a pharmaceutical composition, a foodstuff, a nutrient-containing composition, a vitamin, a nutraceutical, and combinations thereof.
5. The delivery system of claim 1 wherein the encapsulating material is selected from the group consisting of polyvinyl acetate, polyethylene, crosslinked polyvinyl pyrrolidone, polymethylmethacrylate, polylactidacid, polyhydroxyalkanoates, ethylcellulose, polyvinyl acetatephthalate, polyethylene glycol esters, methacrylicacid-co-methylmethacrylate and combinations thereof.
6. The delivery system of claim 1 wherein the encapsulating material is present in an amount of from about 30% to 99% by weight based on the total weight of the delivery system.
7. The delivery system of claim 1 wherein the encapsulating material is present in an amount of from about 60% to 90% by weight based on the total weight of the delivery system.

8. The delivery system of claim 1 wherein the active component is selected from the group consisting of a sweetener, an acid, a flavorant, a pharmaceutical, a therapeutic agent, a vitamin, a breath freshener, a cooling agent and combinations thereof.

9. The delivery system of claim 1 wherein the active component is a high intensity sweetener.

10. The delivery system of claim 8 wherein the active component is a sweetener and is selected from the group consisting of an amino acid based sweetener, a dipeptide sweetener, glycyrrhizin, saccharin, a saccharin salt, an acesulfame salt, a cyclamate, a stevioside, talin, a dihydrochalone compound, a chlorinated sucrose polymer, and combinations thereof.

11. The delivery system of claim 9 wherein the high intensity sweetener is selected from the group consisting of neotame, aspartame, sucralose, and a mixture thereof.

12. The delivery system of claim 8 wherein the active component is present in an amount of from about 1% to 70% by weight based on the total weight of the delivery system.

13. The delivery system of claim 1 wherein the active component is present in an amount of from about 10% to 40% by weight based on the total weight of the delivery system.

14. The delivery system of claim 1 further comprising a tensile strength modifying agent.

15. The delivery system of claim 14 wherein the tensile strength modifying agent is selected from the group consisting of a fat, an emulsifier, a plasticizer, a softener, a low molecular weight polymer, a high molecular weight polymer, a wax, and combinations thereof.

16. The delivery system of claim 14 wherein the tensile strength modifying agent is selected from the group consisting of a hydrogenated oil, a glycerol monostearate, a wax, a low molecular weight polymer, triacetin, glycerin, a rosin ester, and combinations thereof.

17. The delivery system of claim 14 wherein the tensile strength modifying agent is present in an amount of up to 40% by weight based on the total weight of the delivery system.

18. The delivery system of claim 1 in the form of particles or granules.

19. The delivery system of claim 18 wherein the particles or granules have a particle size of up to 600 microns.

20. The delivery system of claim 19 wherein the particles or granules have a particle size of 75 to 600 microns.

21. An edible composition comprising at least one edible composition forming component and a the delivery system of claim 1.

22. The edible composition of claim 21 selected from the group consisting of a chewing gum composition, a food product, a confectionery composition, a pharmaceutical composition, a beverage, a foodstuff, a nutrient-containing composition, a vitamin, a nutraceutical, and a combination thereof.

23. The edible composition of claim 21 wherein the encapsulating material is present in an amount of from about 0.2% to 10% by weight based on the total weight of the edible composition.

24. The edible composition of claim 22, which is a chewing gum composition and wherein the at least one edible forming component comprises a gum base.

25. The edible composition of claim 24 wherein the tensile strength of the delivery system is from about 6,500 psi to 200,000 psi.

26. The edible composition of claim 24 wherein the encapsulating material is present in an amount of from about 30% to 99% by weight based on the total weight of the delivery system.

27. The edible composition of claim 24 wherein the active component is selected from the group consisting of a sweetener, an acid, a flavorant, a pharmaceutical, a therapeutic agent, a vitamin, a breath freshener, a cooling agent and combinations thereof.

28. The edible composition of claim 24 wherein the active component is present in an amount of from about 1% to 70% by weight based on the total weight of the delivery system.

29. The edible composition of claim 24 wherein the encapsulating material further comprises a tensile strength modifying agent.

30. The edible composition of claim 29 wherein the tensile strength modifying agent is selected from the group consisting of a fat, an emulsifier, a plasticizer, a softener, a low molecular weight polymer, a high molecular weight polymer, a wax, and combinations thereof.

31. The edible composition of claim 22, which is a confectionary and which comprises a confectionery carrier.

32. The edible composition of claim 31 wherein the tensile strength of the delivery system is from about 6,500 to 200,000 psi.

33. The edible composition of claim 31 wherein the encapsulating material is present in an amount of from about 30% to 99% by weight based on the total weight of the delivery system.

34. The edible composition of claim 31 wherein the active component is selected from the group consisting of a sweetener, an acid, a flavorant, a pharmaceutical, a therapeutic agent, a vitamin, a breath freshener, a cooling agent, and combinations thereof.

35. The edible composition of claim 31 wherein the active component is present in an amount of from about 1 % to 70% by weight based on the total weight of the delivery system.

36. The edible composition of claim 31 wherein the delivery system further comprises a tensile strength modifying agent.

37. The confectionary edible composition of claim 36 wherein the tensile strength modifying agent is selected from the group consisting of a fat, an emulsifier, a plasticizer, a softener, a low molecular weight polymer, a high molecular weight polymer, a wax, and combinations thereof.

38. A method of preparing a target delivery system for an edible composition comprising combining at least one active component and at least one encapsulating material until a preselected tensile strength of the target delivery system is obtained based on comparison with the tensile strength of at least one sample delivery system having the same or similar active component and a known release rate of the active component.

39. The method of claim 38 further comprising obtaining a preselected tensile strength based on a comparison with a plurality of sample delivery systems.

40. The method of claim 38 further comprising:

(a) obtaining a plurality of sample delivery systems comprising the at least one active component and the at least one encapsulating material wherein each of said sample delivery systems has a different tensile strength;

(b) testing the sample delivery systems to determine the respective release rates of the active component; and

(c) formulating the target delivery system containing the same or similar active component with a tensile strength corresponding to a desired release rate of the active component based on the sample delivery systems.

41. The method of claim 38 wherein the additive is a tensile strength modifying agent.

42. The method of claim 38 wherein the tensile strength of each sample delivery system is at least 6,500 psi.

43. The method of claim 38 further comprising:
determining a desired release rate for the at least one active component in the edible composition;
determining a tensile strength associated with the desired release rate; and
formulating the target delivery system for the at least one active component based, at least in part, on the tensile strength.

44. The method of claim 43, wherein the tensile strength is at least 6,500 psi.

45. The method of claim 43, wherein the target delivery system includes at least one additive.

46. The method of claim 43, further comprising:
associating a different tensile strength for each of a plurality of release rates for each of a plurality of different active components.

47. A method of preparing the delivery system of claim 1, comprising encapsulating the at least one active component in the encapsulating material.

48. A method of preparing an edible composition having at least one active component which releases the at least one active component at a desired release rate, said method comprising

encapsulating the at least one active component in at least one encapsulating material to form a target delivery system having a tensile strength of at least 6,500 psi; and adding the target delivery system to the edible composition.

49. A method of selecting at least one delivery system suitable for incorporation into an edible composition, each of said delivery systems comprising an active component encapsulated within an encapsulation material, said method comprising:

determining a desired release rate for a first active component in the edible composition;

determining a first desired tensile strength for a first delivery system associated with said desired release rate; and

selecting a first delivery system for first said active component based, at least in part, on said first tensile strength.

50. The method of claim 49 further comprising:

determining a second desired release rate for a second active component in the edible composition;

determining a second desired tensile strength for a second delivery system associated with said second desired release rate; and

selecting a second delivery system for said second active component based, at least in part, on said second tensile strength.

51. The method of claim 50 further comprising repeating the steps of determining a desired release rate, determining a desired tensile strength and selecting a delivery system for at least one additional active component of the edible composition.

52. The method of claim 51, wherein the tensile strength is at least 6,500 psi.

53. The method of claim 51, wherein the delivery system further comprises at least one additive.

54. The method of claim 53, wherein the additive is a tensile strength modifying agent.

55. The method of claim 51, wherein determining the desired tensile strength comprises:

associating a different tensile strength for each of a plurality of release rates of said at least one active component.

56. The method of claim 55, wherein determining the desired tensile strength comprises:

associating a different tensile strength for each of a plurality of release rates for each of the plurality of active components.

57. The method of claim 55, further comprising:

determining a desired tensile strength for each of a plurality of delivery systems.

58. A method of preparing a target delivery system for an edible composition useful for delivering at least one active component at a desired release rate, said method comprising encapsulating the at least one active component in an encapsulating material in a manner that provides the target delivery system with a target tensile strength associated with the desired release rate, enabling the delivery system to release the at least one active component from the edible composition at the desired release rate.

59. The method of 58 wherein the target tensile strength is at least 6,500 psi.

60. The method of claim 59 comprising:

- a) determining the desired release rate of the active component;
- b) determining the target tensile strength of the delivery system capable of delivering the at least one active component at the desired release rate; and
- c) formulating the target delivery system containing the at least one active component having the target tensile strength.

61. A method of preparing an edible composition containing a target delivery system useful for delivering at least one active component at a desired release rate, said method comprising encapsulating the at least one active component in an encapsulating material in a manner that provides the target delivery system with a target tensile strength associated with the desired release rate enabling the delivery system to release the at least one active component from the edible composition at desired release rate, and adding the target delivery system to the edible composition.

62. The method of Claim 38, which further comprises combining at least one additive with the at least one active component and at least one encapsulating material.

63. The delivery system of claim 1 wherein the tensile strength of the delivery system is at least about 10,000 psi.

64. The delivery system of claim 1 wherein the tensile strength of the delivery system is at least about 22,000 psi.

65. The delivery system of claim 1 wherein the tensile strength of the delivery system is at least about 24,000 psi.

66. The delivery system of claim 1 wherein the tensile strength of the delivery system is at least about 42,000 psi.

67. The edible composition of claim 21, which comprises at least two delivery systems.

68. The edible composition of claim 67, wherein each of the at least two delivery systems comprise at least two different active component.

69. The edible composition of claim 67, wherein at least one active agent is a sweetener and a second active agent is a flavorant.

70. The edible composition of claim 66 wherein each of the at least two delivery systems has a different tensile strength.

71. A chewing gum composition, comprising a gum base and at least one active component encapsulated within a polymer encapsulating material, wherein the active component is released for at least 15 minutes following the start of chewing the composition.

72. The chewing gum composition of claim 71, wherein the active component is released for at least 20 minutes following the start of chewing the composition.

73. The chewing gum composition of claim 71, wherein the active component is released for at least 30 minutes following the start of chewing the composition.

74. The chewing gum composition of claim 71, wherein the release of the active component varies during the at least 15 minutes.

75. The chewing gum composition of claim 71, wherein the at least one active component encapsulated within a polymer encapsulating material has a tensile strength of above 6,500 psi.

76. The chewing gum composition of claim 71, wherein the at least one active component encapsulated within a polymer encapsulating material has a tensile strength of above 10,000 psi.

77. The delivery system of claim 16, wherein the tensile strength modifying agent is a fat.

78. The delivery system of claim 77, wherein the fat is present in an amount up to 5% by weight of the delivery system.

79. The delivery system of claim 14, wherein the tensile strength modifying agent is an oil.

80. The delivery system of claim 79, wherein the oil is present in an amount up to 5% by weight of the delivery system.

81. The delivery system of claim 14, which comprises two tensile strength modifying agents and the tensile strength modifying agents are a fat and an oil.

82. The delivery system of claim 80, wherein the combination of fat and oil is present in an amount up to 5% by weight of the delivery system.

83. A chewing gum composition, comprising a gum base and at least one sweetener encapsulated within a polymer encapsulating material, wherein the sweetener is perceived by a consumer for at least 15 minutes following the start of chewing the composition.

84. The chewing gum composition of claim 83, wherein the sweetener is perceived by the consumer for at least 20 minutes following the start of chewing the composition.

85. The chewing gum composition of claim 83, wherein the sweetener is perceived by the consumer for at least 30 minutes following the start of chewing the composition.

86. The chewing gum composition of claim 83, wherein the at least one active component encapsulated within a polymer encapsulating material has a tensile strength of above 6,500 psi.

87. The chewing gum composition of claim 83, wherein the at least one active component encapsulated within a polymer encapsulating material has a tensile strength of above 10,000 psi.

88. The edible composition of claim 33, wherein the encapsulating material is present in an amount of from about 60 % to 90% by weight based on the total weight of the delivery system.

89. The edible composition of claim 35, wherein the active component is present in an amount of from about 10 to 40 % by weight based on the total weight of the delivery system.

90. The edible composition of claim 89, wherein the active component is present in an amount of from about 0.1 to 6 % by weight based on the total weight of the delivery system.

91. The edible composition of claim 89, wherein the active component is present in an amount of from about 0.5 to 3 % by weight based on the total weight of the delivery system.

92. A chewing gum composition, comprising at least one gum base, a delivery system and at least one active component encapsulated within the delivery system, wherein the delivery system comprises at least one additive in an amount sufficient such that at least about 50% of the at least one active component is maintained within the delivery system for at least 15 minutes from the start of chewing the chewing gum composition.

93 . A chewing gum composition, comprising at least one gum base, a delivery system and at least one active component, wherein the at least one active agent is released from the delivery system at a rate of at least about 25% after 15 minutes from the start of chewing the chewing gum composition.

94. A delivery system, which comprises at least one encapsulating material, at least one active component, and at least one additive, wherein the at least one additive is present in the delivery system in an amount sufficient such that the at least one active agent is released at a rate of 25 % over the course of 15 minutes from delivery.

Figure 1: Human Panel sensory results – Sweetness Intensity

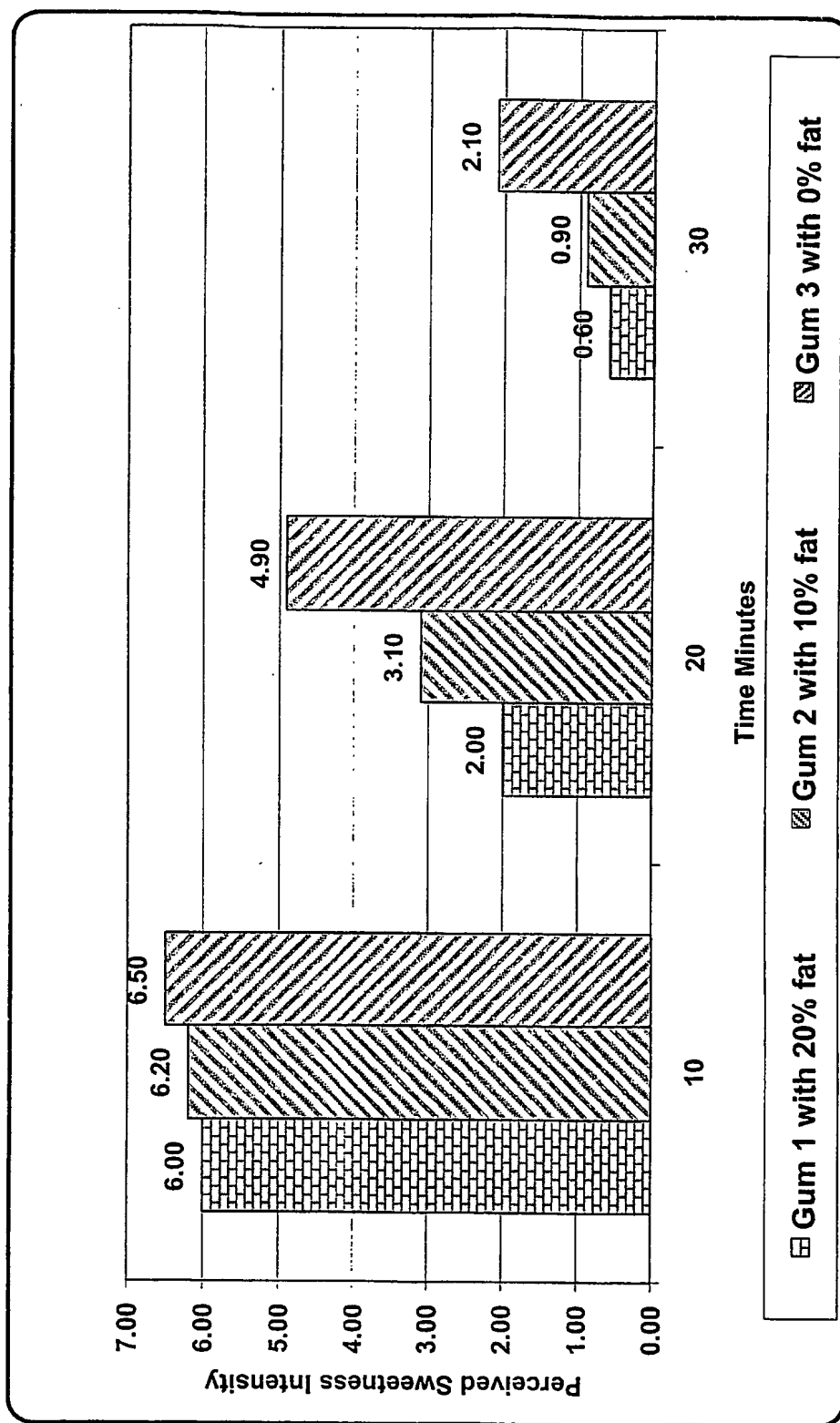


Figure 2: Human Panel sensory results – Sweetness Intensity

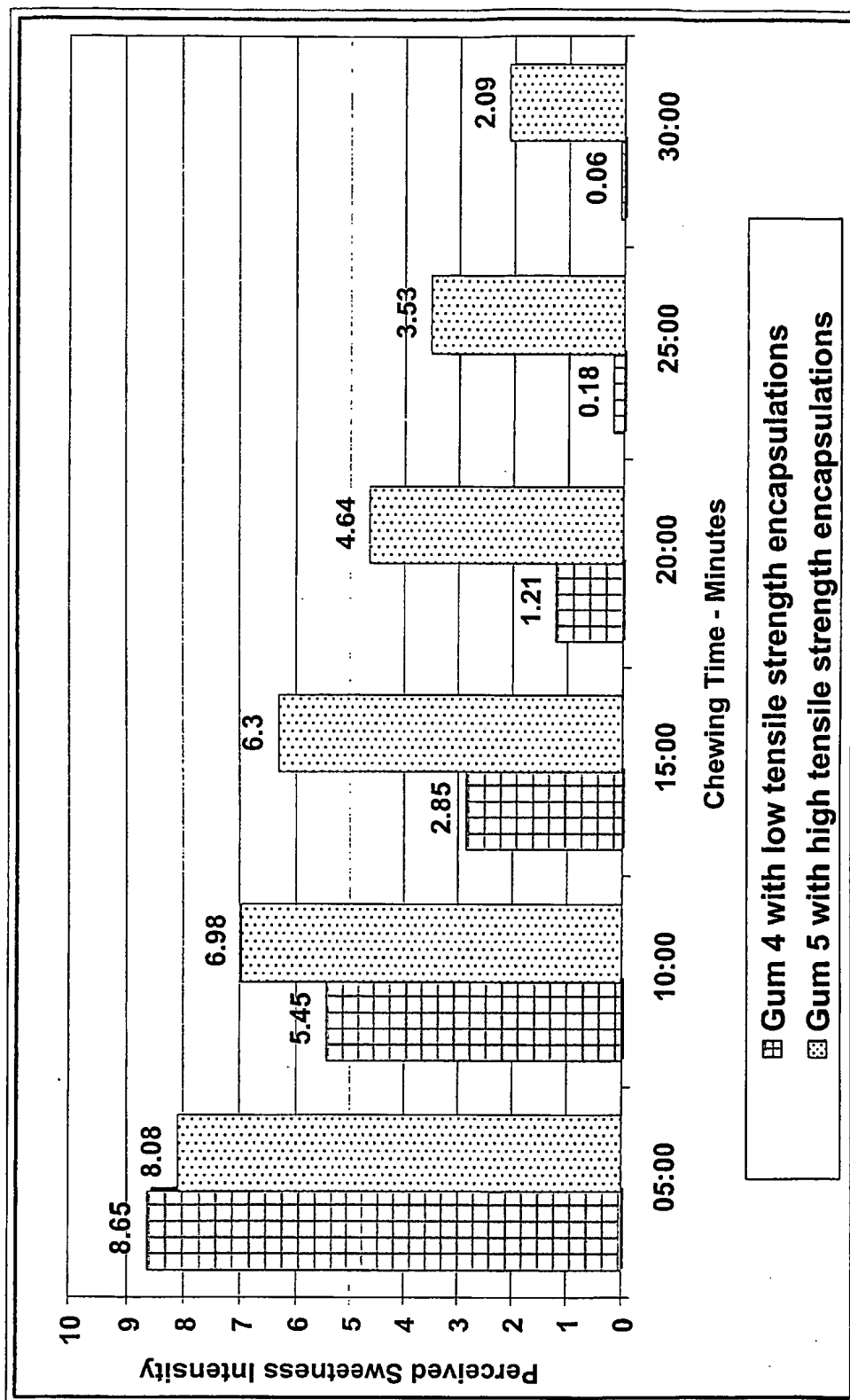


Figure 3: Human chew-out / residual Aspartame in chewed cud

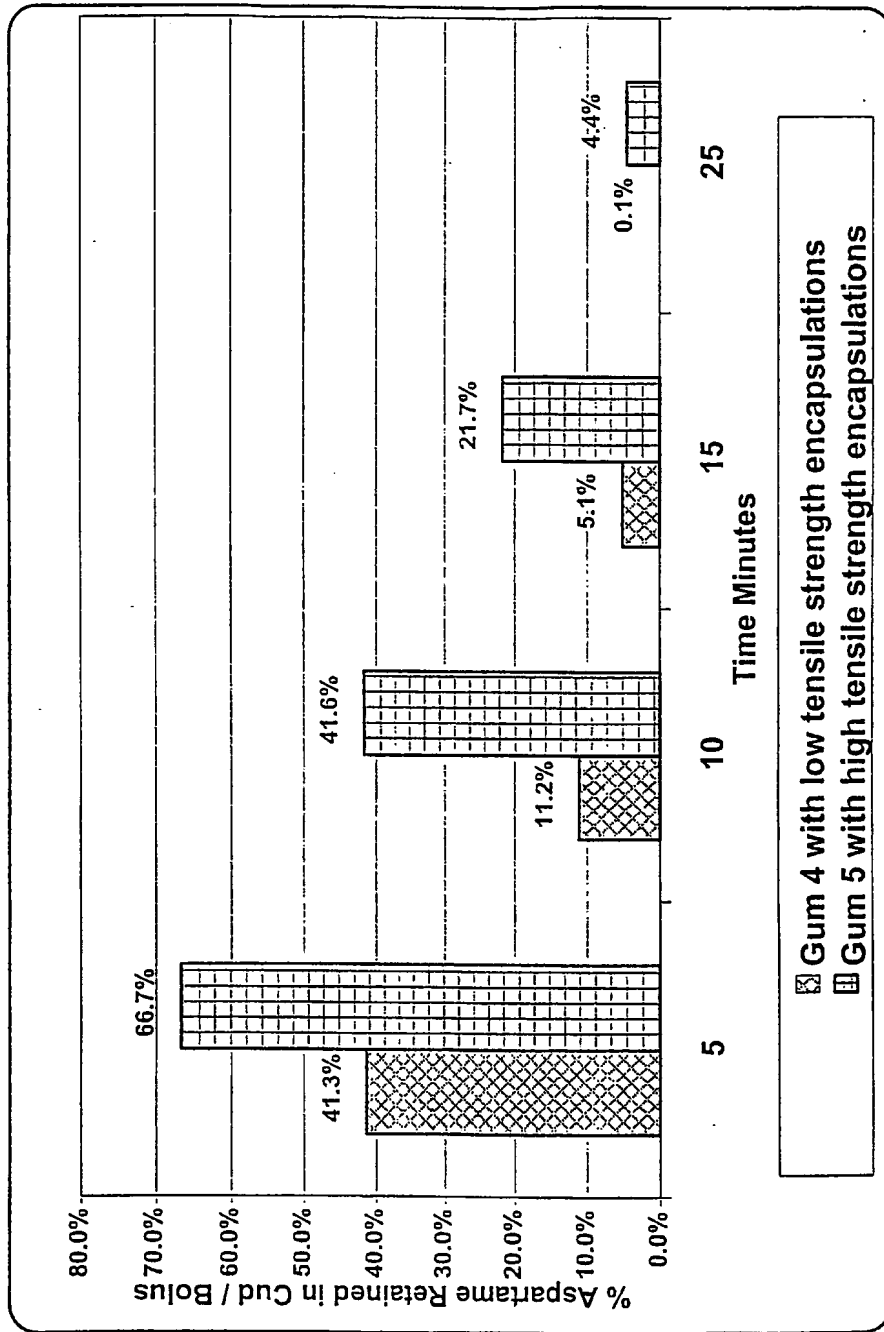
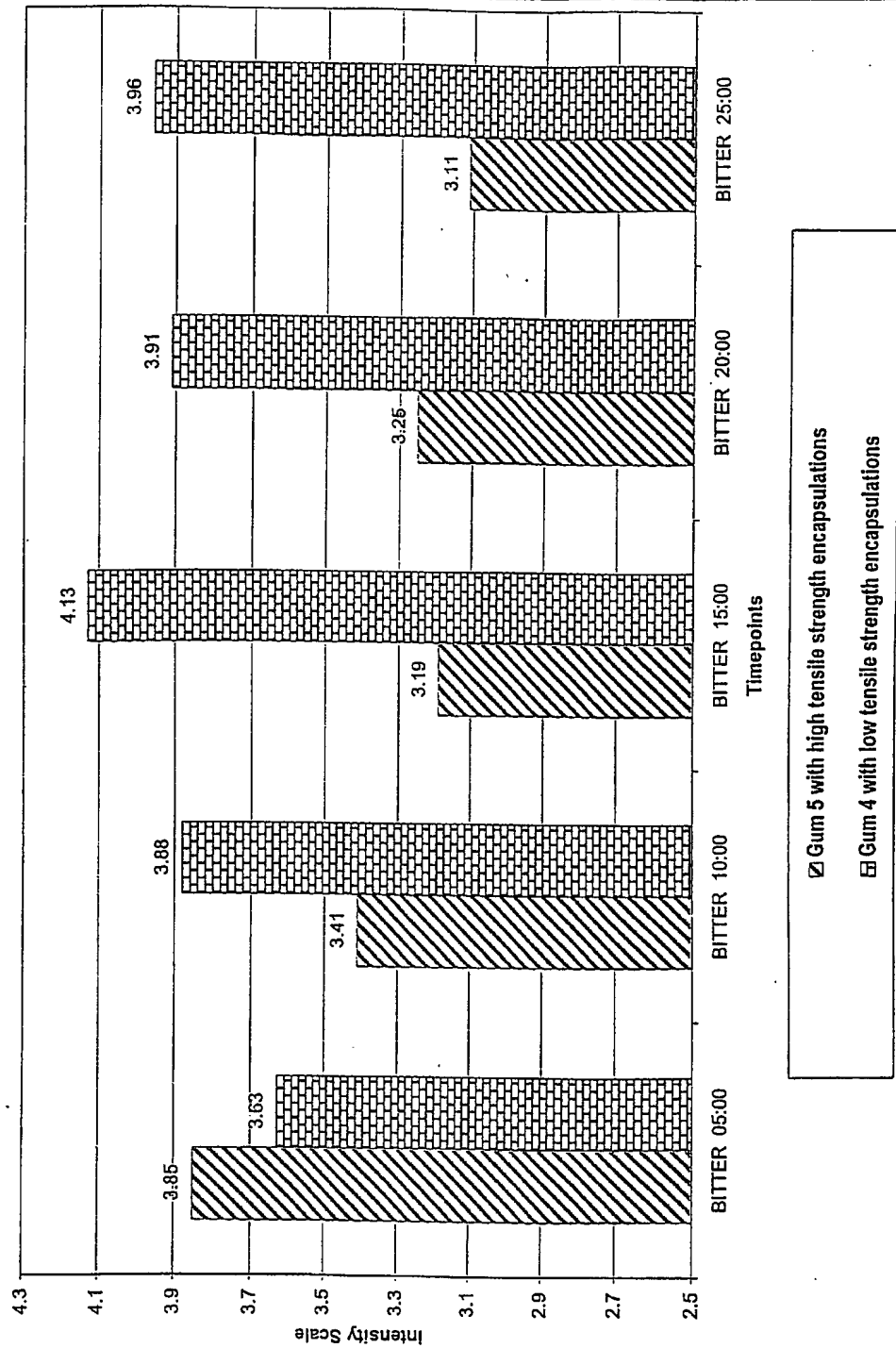


Figure 4: Human Panel Sensory results - Bitterness Intensity



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/37185

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 47/00
US CL : 424/400, 4334, 439

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/400, 4334, 439

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|--------------|--|--|
| X -- Y | JP 02083030 A (LION CORP) 23 March 1990 (23.03.1990), see abstract. | 1-4,6-8,14, 18-36, 47-48, 58-59,61-66,71-76 and 92-94 ----- 1-94 |
| Y | US 5,198,251 A (SONG et al.) 30 March 1993 (30.03.1993), see entire document. | 1-94 |

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents.

"A" document defining the general state of the art which is not considered to be of particular relevance

"B" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

21 March 2005 (21.03.2005)

Date of mailing of the international search report

10 MAY 2005

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer,

Lakshmi S. Channavajjala

Telephone No. 703-308-1235